Assessing Real-world Natural History of Indolent Systemic Mastocytosis: A Retrospective Matched Cohort Study from Mayo Clinic Electronic Health Records

Thanai Pongdee[1], Dakota Powell[2], Taylor Weis[2], Robyn Scherber[2], Allison Smither[3], Purushotham K[3], Katherine Carlson[3], Prerna Singh[3], Jamie Lo[3], Nivedita Rangarajan[3], Erin Sullivan[2], Hannah Barman[3]

[1]Division of Allergic Diseases, Mayo Clinic, Rochester, Minnesota

[2]Blueprint Medicines Corporation, Cambridge, Massachusetts

[3]nference, Inc., Cambridge, Massachusetts

Presented at AAAAI 2025
San Diego, CA, USA

Evaluating the real-world disease burden and natural history of ISM compared to a propensity-matched control cohort

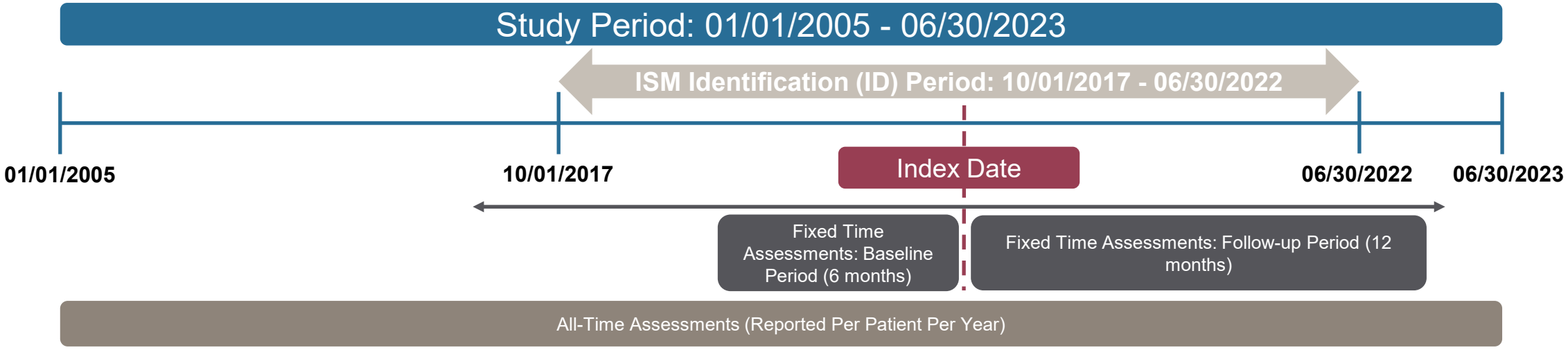
Background

- Systemic mastocytosis (SM) is a clonal mast cell disease primarily driven by the KIT D816V mutation in ~95% of cases.[1]
- ISM is the most common SM subtype, accounting for over 80% of all cases of SM.[2,3]
- ISM patients often experience severe, unpredictable, and debilitating skin, gastrointestinal (GI), and systemic symptoms, including potentially life-threatening anaphylactic reactions.[4-6]
- Uncontrolled symptoms may worsen over time and can result in patients developing comorbid conditions.[7-11]
- These symptoms lead to deterioration of patient quality of life, including impairment of daily activities, mood, and ability to work, and increased use of healthcare resources.[4-6]

References:
1. Bose P et al. Avapritinib for systemic mastocytosis. *Expert Rev Hematol*. Aug 2021;14(8):687-696. doi:10.1080/17474086.2021.1959315
2. Cohen SS et al. Epidemiology of systemic mastocytosis in Denmark. *Br J Haematol*. Aug 2014;166(4):521-8. doi:10.1111/bjh.12916
3. Ungerstedt J et al. Clinical outcomes of adults with systemic mastocytosis: A 15-year multidisciplinary experience. *Cancers (Basel)*. Aug 16 2022;14(16)doi:10.3390/cancers14163942
4. Zeiger RS et al. Patient reported burden of indolent systemic mastocytosis in a managed care organization. *J Allergy Clin Immunol Pract*. Jan 2025;13(1):202-212.e7 doi:10.1016/j.jaip;/2024.10.021
5. Tse KY et al. MASTering systemic mastocytosis: Lessons learned from a large patient cohort. J Allergy Clin Immunol: Global. Nov 2024; 3(4):100316. doi: 10.1016/j.jacig.2024.100316
6. Triggiani M et al. The burden of indolent systemic mastocytosis in Europe: Results from the PRISM patient survey. Oral presentation presented at: EAACI; 02 June 2024; Valencia, Spain.
7. Mesa RA et al. Cancer. 2022;128:3691–3699
8. Hermine O et al. PLoS One. 2008;3:e2266
9. van Anrooij B et al. Allergy. 2016;71:1585–1593
10. Akin C et al. J Allergy Clin Immunol. 2022;149:1912–1918
11. Hartmann K et al. J Allergy Clin Immunol. 2016;137:35–45

Design: matched, retrospective, cohort study

Source	De-identified, retrospective data queried from the Mayo Clinic EMR database (all Mayo Clinic sites in the US): • Rochester, Minnesota • Phoenix/Scottsdale, Arizona • Jacksonville, Florida • Mayo Clinic locations in Minnesota, Iowa, and Wisconsin
Curation	Structured EMR data extraction and use of natural language processing (NLP) to review unstructured clinical notes
Assessment	Patient demographics, diagnostic workup (for ISM patients), symptoms, comorbidities, healthcare resource use, medication use
Approach	Employs a control cohort matched (10:1) on demographic and clinical characteristics



Index Date

- First observed ISM diagnosis (by ICD code or identification with NLP) serves as the Index date for the ISM cohort.
- The matched control cohort uses the first encounter that is at least 6 months after 2 prior encounters during the study period as the index date.

Innovative application of AI methods allows for the collection of more varied data elements than traditional analysis

SUBJECTIVE HISTORY OF PRESENT ILLNESS: [redacted] returns for followup of indolent systemic mastocytosis. Recall that she has about 5 % involvement of the bone marrow. She was doing quite well, exercising regularly and carrying on with her normal activities, until an episode of COVID in February. Following about a 2-week course of COVID, she developed a generalized reaction with rash, palpitations, angioedema, diffuse musculoskeletal pains, and itching. She developed confluent areas of hives on the skin which did not respond to Benadryl. She may have lost consciousness in addition. She did not use her EpiPen, however. She was seen in an emergency room setting and treated with intravenous steroids and was given a 2-week course of tapering prednisone which ended in March. Since that time, she has nearly fully recovered from this spell. She feels that she flushes easier at this time. Her skin has cleared, however. She has had no digestive issues, lymphadenopathy, or fevers. She did have a bone density done today. She has had no skeletal complaints or fractures.

Clinical Encounter Note Examples	Data Label
Patient returns for followup of indolent systemic mastocytosis	**Has disease**
Diagnosis of systemic mastocytosis pending tryptase levels and KIT mutation testing	Maybe/unknown
The KIT D816V mutation is associated with SM	Other
Based on the workup and normal serum tryptase and LTE4 levels I do not believe this patient has ISM	Does not have disease

To Supplement Structured Data Review, Natural Language Processing (NLP) was Used for Additional Data and Context

203 eligible patients with ISM were identified and propensity score matched with 2,030 similar patients without ISM

7M+ Patient Lives in Mayo Clinic system

931 Patients with Evidence of ISM during study Period

Patients must have at least one diagnosis of ISM any time before 6/30/2023, the cutoff for data availability for the study; Diagnosis determined by patients with at least one ICD code for SM (D47.02) with ISM determined via use of SM subtyping algorithm ***or*** NLP-detected ISM

384 Patients Meet Inclusion/Exclusion Criteria

Inclusion Criteria:
- ≥2 patient visits with medical record information during *baseline* period
- ≥1 patient visits with medical record information during *follow-up* period
- Adults (≥ 18 years old) on the index date

Exclusion Criteria:
- Clinical trial participation during baseline or follow-up periods
- Evidence of AdvSM* during the pre-index or baseline period

203 Patients in Final ISM Cohort

Patients with ISM diagnosis between 1/1/2005-6/30/2022 and at least one record in ID window (10/1/2017 - 6/30/2022)

2,030 Matched Control Patients

Propensity score matched 10:1,
Matching characteristics:
- Race
- Ethnicity
- Sex
- Age at index
- Quan-CCI Score
- BMI at index
- Smoking status

AdvSM: Advanced systemic mastocytosis; CCI: Charlson comorbidity index; ISM: Indolent systemic mastocytosis
*Evidence of AdvSM includes evidence of diagnostic coding for mast cell leukemia, mast cell neoplasms, or other hematologic neoplasms

ISM patient demographics, diagnosis, and high symptom burden

Demographics

Total participants: **203**
Mean age: **51.4 years**
Female: **66.5%**

Average Length of follow-up: **4.4 years**

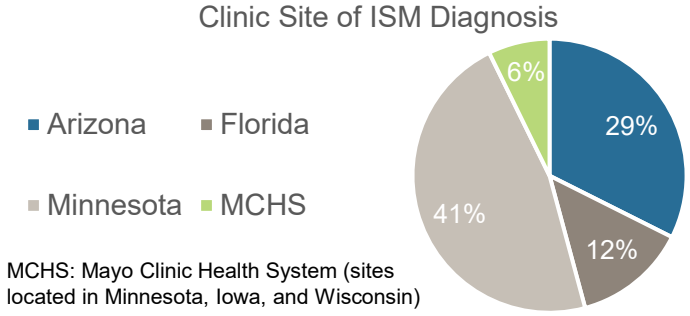
Race and Ethnicity

White: **93%**

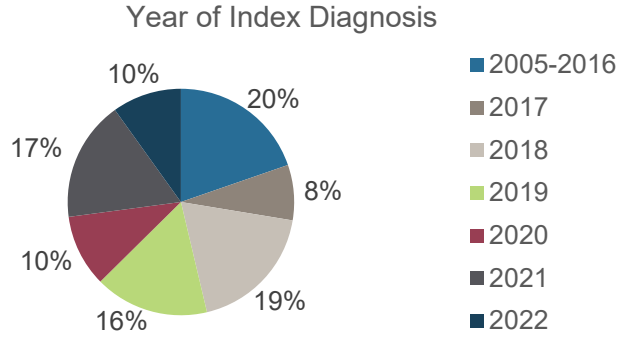
Black or African American, Asian, Other/Unknown: **7%**

Hispanic or Latino: **5%**

Diagnosis



MCHS: Mayo Clinic Health System (sites located in Minnesota, Iowa, and Wisconsin)



Symptoms

Average number of distinct symptoms reported:

10.6 Baseline

13.3 Follow-up

Prevalence of most reported symptoms during 6-month baseline:

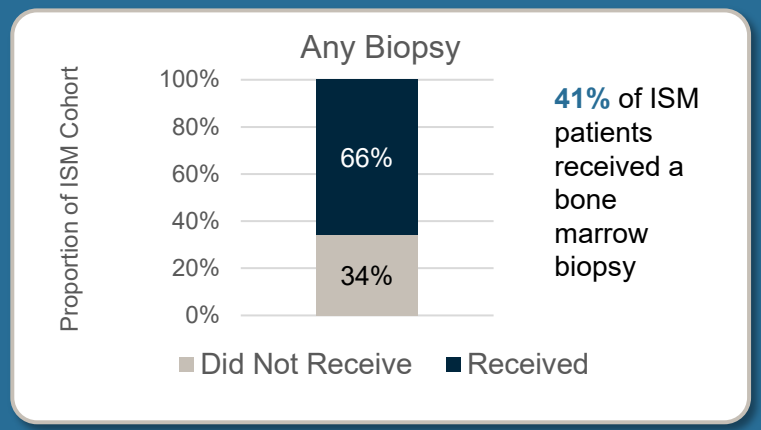
Allergic Reaction: **58%**
Lymphadenopathy: **57%**
Diarrhea: **54%**
Dyspnea: **53%**
Nausea: **53%**
Fatigue: **52%**
Dermatologic*: **66%**

At time of diagnosis, ISM patients present with numerous, burdensome, and heterogenous symptoms that increase following diagnosis.

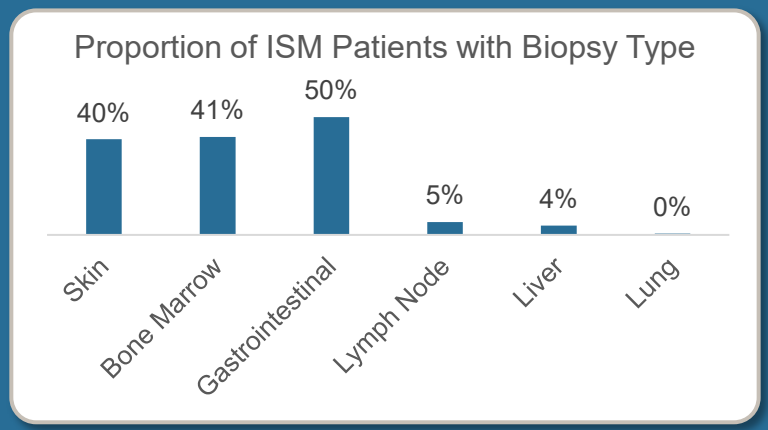
ISM: Indolent Systemic Mastocytosis
*Dermatologic symptoms include angioedema, flushing, cutaneous mastocytosis, pruritic, urticaria.

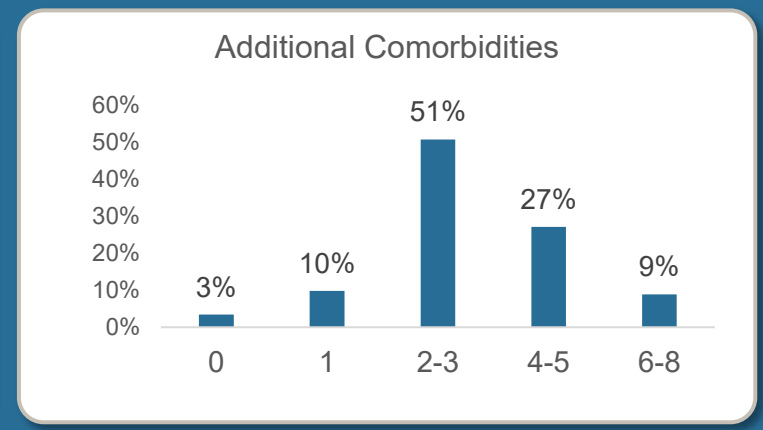
Real-world diagnosis of patients with ISM

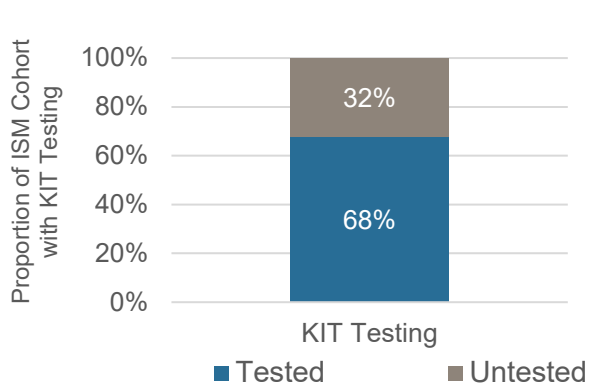
SM Workup

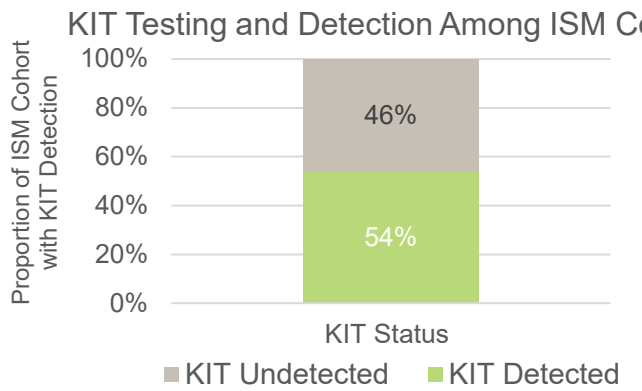


41% of ISM patients received a bone marrow biopsy









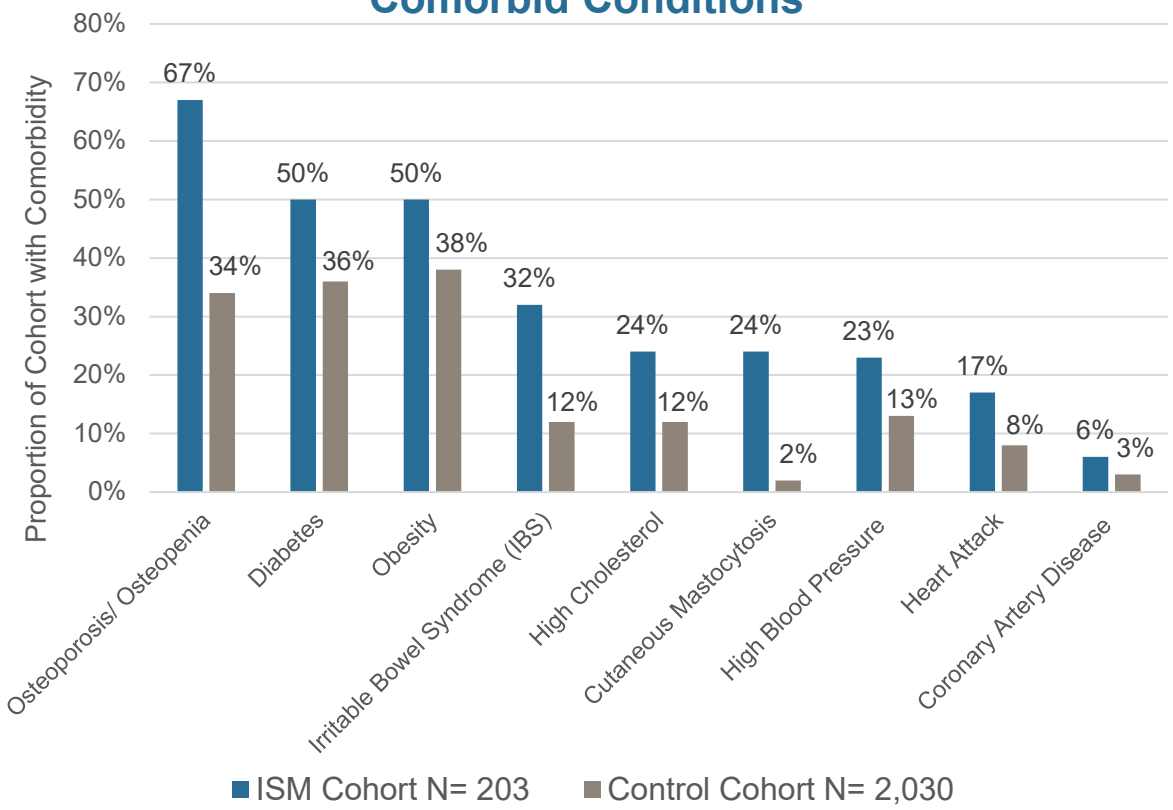
Most testing occurred prior to the widespread availability of high-sensitivity KIT testing

Disease awareness, education, and high sensitivity testing for KIT D816V can assist in the proper workup of ISM and is a critical tool enabling accurate diagnosis.

Note: Even with mixed methodology using structured EMR data and NLP, specific information related to testing and diagnostic workup that occurred outside of the Mayo system may not end up in clinical notes.

Significantly higher rates of comorbid conditions in ISM patients compared to matched controls

Proportion of Cohort with Specified Comorbid Conditions



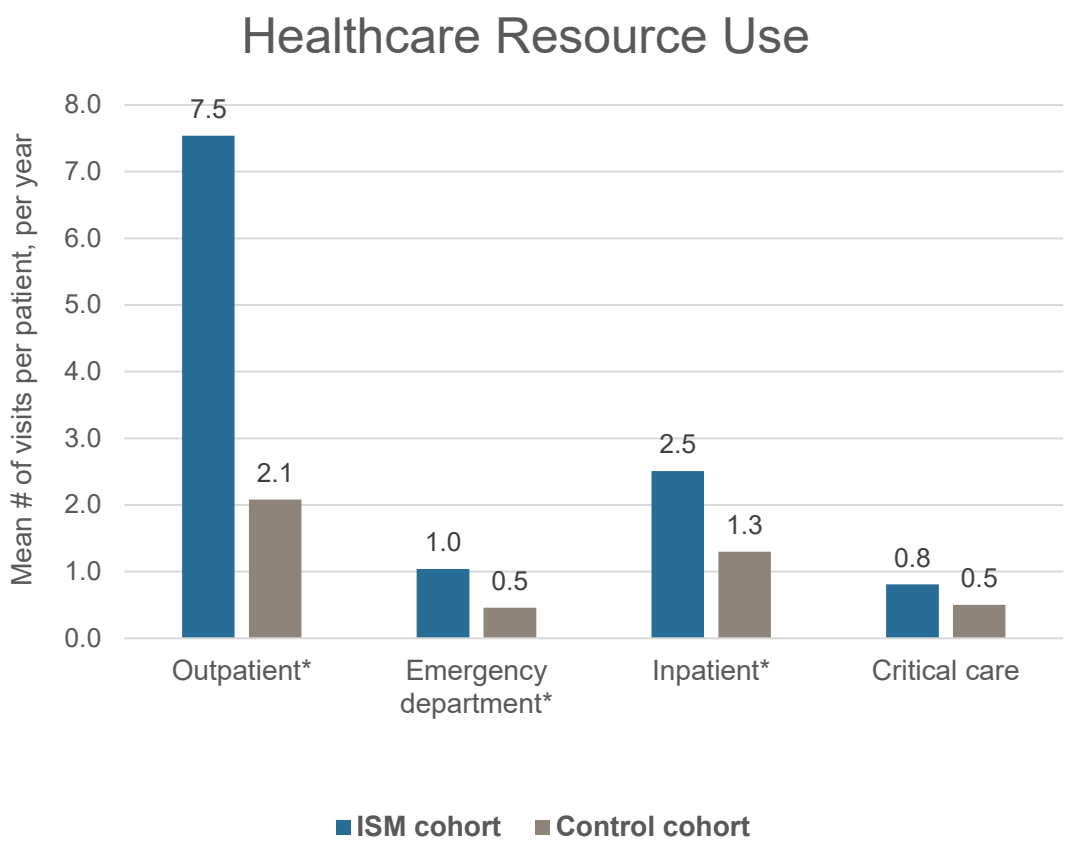
	χ^2 test p-value		χ^2 test p-value
Osteoporosis/ Osteopenia	**<0.0001**	Cutaneous Mastocytosis	**<0.0001**
Diabetes	**0.0001**	High Blood Pressure	**0.0001**
Obesity	**0.0008**	Heart Attack	**<0.0001**
Irritable Bowel Syndrome (IBS)	**<0.0001**	Coronary Artery Disease	**0.0220**
High Cholesterol	**<0.0001**		

Proportion of Cohort with Specified Allergies

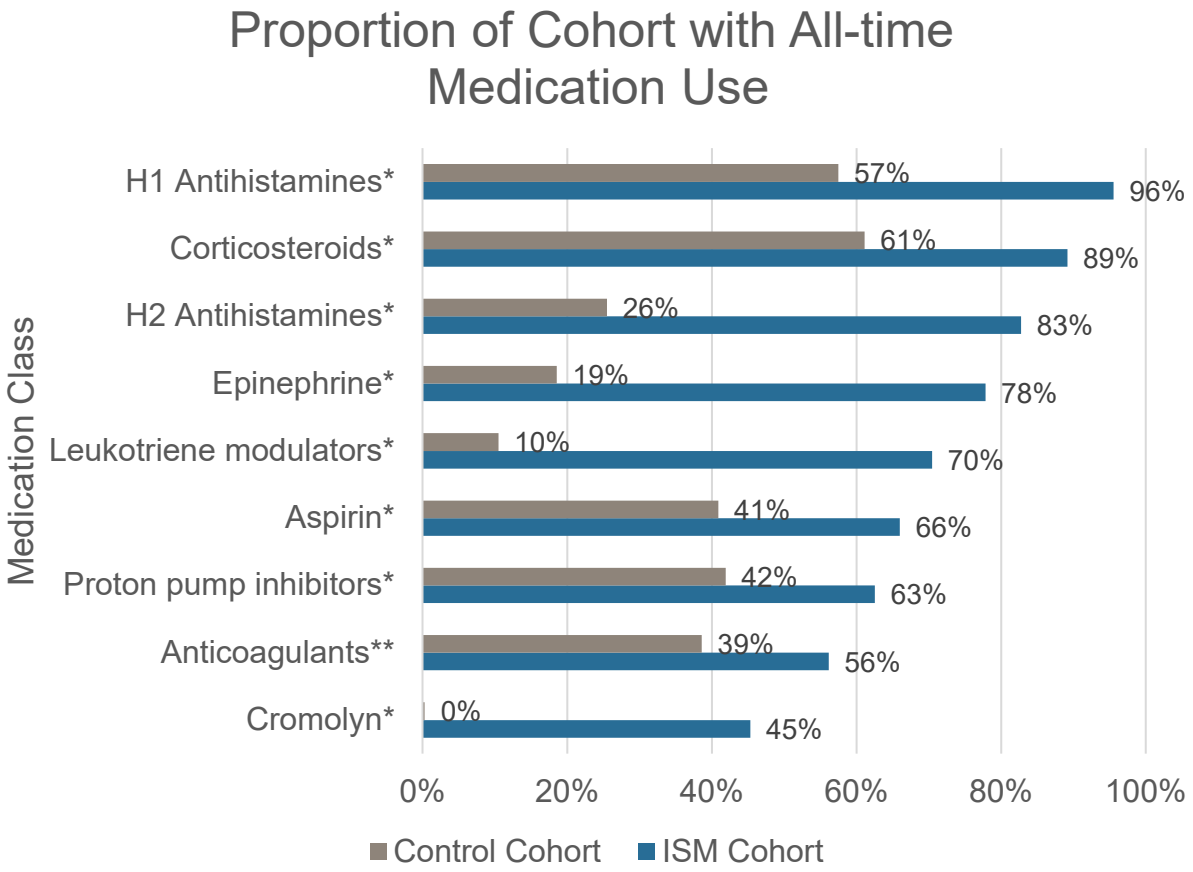
	ISM Cohort N= 203	Control Cohort N= 2,030	χ^2 test p-value
Food	24%	7%	**<0.0001**
Environmental	9%	5%	**0.0159**
Drug Allergies	8%	4%	**0.0078**
Stinging Insect	7%	1%	**<0.0001**
Latex	7%	3%	**0.0026**
Radiocontrast	5%	1%	**<0.0001**
Dander/pet	3%	1%	**0.0120**
Venom	<1%	<1%	0.3922

Patients with ISM are **more likely to have allergies**, including food (24% vs 7%) and stinging insect [hymenoptera] (7% vs 1%)

Significantly higher rates of healthcare and medication utilization in ISM patients compared to matched controls



Note that emergency department visits are likely under reported in this data, as patients may seek emergency care outside of the Mayo Clinic system.



Patients with ISM take **more classes of medications** compared to control patients (14.68 vs 5.79)

Statistical significance – χ^2 test: *p-value <0.001; **p-value = 0.001

Conclusions

- This study employed innovative methods combining structured data and unstructured data captured using NLP, providing deeper insight into patient symptoms and burden than traditional data alone.
- Patients with ISM present with multiple, diverse, and burdensome symptoms that increase in prevalence over time.
- This heterogeneous presentation complicates timely diagnosis that may be improved with disease education and high sensitivity testing.
- Patients with ISM were more likely to have serious comorbidities, including being twice as likely to have osteoporosis/osteopenia and key cardiovascular diseases.
- Patients with ISM had significantly higher rates of medication use and healthcare services, including inpatient stays, outpatient visits, emergency department visits, compared to the matched cohort.